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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/726,624 | 11/30/2000 | Min Li | 01107.00063 | 1501 |

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BANNER & WITCOFF
1001 G STREET N W
SUITE 1100
WASHINGTON, DC 20001

| EXAMINER | |
|---|---|
| PONNALURI, PADMASHRI | |
| **ART UNIT** | **PAPER NUMBER** |
| 1639 | 13 |

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/726,624 | Min Li |
| **Examiner** | **Art Unit** |
| Padmashri Ponnaluri | 1639 |

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on *Aug 11, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *1, 5, 9, 17, 22, 45-51, 53-63, and 65-75* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 5, 9, 17, 22, 45-51, 53-63, and 65-75* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

1. The amendment D filed on 8/11/03 has been fully considered and entered into the application.

2. New claims 70-75 have been added by amendment D filed on 8/11/03.

3. Claims 1, 5, 9, 17, 22, 45-51, 53-63, 65-75 are currently pending in this application.

4. This application has been filed with informal drawings. If applicant renumber the figures, applicant is encouraged to amend the specification so that the description of renumbered figure corresponds to the renumbered figures.

5. The obviousness-type double patenting rejection of record has been withdrawn tin view of applicants arguments that in the parent application these claims were restricted out.

6. The rejection of claims 1, 5, 9, 45-51, 53, 55-56 under 35 U.S.C. 102(b) as being anticipated by US Patent 5,270,170 (Schatz et al) set forth in the previous office action (mailed on 2/25/03) has been maintained for the reasons of record.

7. The rejection of claims 1, 5, 9, 17, 22, 45-51, 53, 55, 56, 58-63, 65, 67-68 and newly added claims 70-75 under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,270,170 (Schatz et al ) and Barbas, III et al (US Patent 6,242,568, filing date 01/1998) in view of the specification disclosure, set forth in the previous office action (mailed on 2/25/03) has been maintained for the reasons of record.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 5, 7, 9, 17, 22, 45-51, 55-56, 58-63, 67-68 and 70-75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection..

The instant claims briefly recite a method of detecting the presence of a polypeptide in a sample comprising contacting the sample with a homogenous population of a detctable virus expressing on its surface a ligand for the polypeptide and detecting the bindign of the virus to the sample.

The specification discloses NMDA as the polypeptide in the sample and the ligands for the polypeptide in the sample is Mag -4.1 or Mag -4.2, which are known to be the ligands for the specific polypeptide. Thus in the claimed method a known pair of ligand and polypeptide are used. The specification disclosure of use of Mag proteins in identifying NMDA receptors in the sample clearly do not provide an adequate representation regarding the open ended claimed method of identifying the presence of any plypeptide in a sample as in the presently claimed invention.

The specification discloses recombinant bacteriophage cells expressing the fusion proteins of the ligands (Mag proteins) and coat proteins on the surface, and use of the bacteriophage in detecting specific NMDA proteins in the sample, which meets the written description. However, the instant claims are open to the use of any viral vectors, however the specification discloses only

the use of bacteriophage and pVIII coat protein to express the fusion proteins. None of these meet the written description provision of 35 U.S.C 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of bacteriophage expressing the fusion proteins of pVIII coat protein and Mag proteins, and the use of the bacteriophage expressing the fusion proteins in the mehtod of detecting the NMDA receptors in the sample, the skilled artisan cannot envision the method of using the other viral vectors and use of the viral vectors in detecting any other proteins in the sample. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only bacteriophage vectors expressing the Mag proteins as fusion proteins and use of the bacteriophage vectors in the mehtod of detecting NMDA receptors, but not the full breadth of the claim meet the written description provision of 35 U.S.C 112, first paragraph.

10. Claims 1, 5, 9, 17, 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey

to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The new limitation 'homogenous population' claimed in claims 1, 5, 9, 17, 22 has no clear support in the specification and the claims as originally filed. The subject matter claimed in claims 1, 5, 9, 17, 22 broadens the scope of the invention as originally disclosed in the specification.

If applicants disagree, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the specification.

11. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

12. Claims 1, 5, 9, 45-51, 53, 55-56 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,270,170 (Schatz et al).

The instant claims briefly recite a method of detecting the presence of a polypeptide in a sample comprising contacting the sample with a detectable virus expressing on its surface a ligand for the polypeptide and detecting binding of the virus to the sample.

US Patent 5,270,170 teaches peptide libraries and screening method. The reference teaches that the screening method of the invention comprises lysing the cells transformed with the peptide library, contacting the fusion proteins of the peptide library with a receptor and isolating the vector that encodes the peptide that binds to the receptor. The reference also teaches the use of fluorescence-activated cell sorter to identify the peptide. The reference teaches once a peptide ligand of interest has been identified, a variety of techniques can be used to diversify a peptide library to construct ligands with improved properties (see column 15). The reference teaches that the degenerate oligonucleotides encoding the ligand are cloned into the random peptide library expression vector to produce variations of starting peptide sequences, and the method is useful for expanding diversity (see column 15) (refers to the instant claim 5). The

reference teaches that the receptor (polypeptide of the instant claims) refers to a molecule that has affinity for a given ligand, and the receptor can be a naturally occurring and can be in an unaltered state or as aggregates with other species (see column 4) (refers to the sample of the instant claims). The reference further teaches that sera, fluids, tissues or cell from patient with disease can be used in the present screening method to identify peptides (see column 5). The reference clearly anticipates the claimed invention.

13. Applicant's arguments filed on 8/11/03 regarding the rejection of claims over Schatz et al have been fully considered but they are not persuasive.

Applicants argue that the reference does not teach homogenous population of detectable virus, which is considered as new matter in the absence of applicants reference to the support for the limitation in the specification.

Applicants argue that the reference does not employ a detectable virus expressing the ligand on its surface. Applicants arguments have been fully considered and are not persuasive, since the instant specification in page 7 discloses that 'the virus utilized in the method can be bacteriophage.'. And Schatz et al in column 4 discloses the 'recombinant DNA vector' refers to a DNA or RNA molecule that encodes a useful function and can be used to transform a host cell.' The reference further discloses that the recombinant DNA vector typically is a phage or plasmid. Thus, the reference clearly teaches the use of bacteriophage vectors.

Applicants argue that Schatz et al does not teach the steps of contacting the virus with a sample detecting the presence of a polypeptide in the sample by virus binding to the sample. Applicants argue that Schatz screens a heterogenous peptides binding to a receptor. Applicants arguments are not persuasive, since the reference teaches that if the 'antigen is unknown, such as

with auto immune diseases, for example, sera fluids, tissue, or cell from patients with disease can be used in the present method to identify the peptides. Further the reference teaches that the present method can be used to tailor a peptide to a particular purpose, and once the peptide is identified, that peptide can serve as basis for developing diagnostic assay . Thus the reference method of use of bacteriophage vectors expressing ligands (peptides) (unknown) which are specific to a receptor (polypeptide in the sample) (known) in a method of identifying ligands which bind to the receptor, and use the identified ligands in a further assays would clearly anticipate the instant claimed method of identifying the presence of a polypeptide in the sample by contacting the sample (polypeptide) (unknown) with bacteriophage expressing the ligands (known) to the polypeptide.

14. Claims 1, 5, 9, 17, 22, 45-51, 53, 5556, 58-63, 65, 67-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,270,170 (Schatz et al ) and Barbas, III et al (US Patent 6,242,568, filing date 01/1998) in view of the specification disclosure.

Schatz et al has been discussed supra.

The claimed invention differs from the prior art teachings by reciting bacteriophage expressing more than 10 copies of the ligand on its surface. Schatz et al do not teach that more than 10 copies of ligand are displayed on the surface of the phage. However, Barbas, III et al teach that mature phage contain 2500 to 3000 copies of VIII coat protein. And the instant specification discloses that the ligand can be encoded by pIII or pVIII coat protein which is standard in the art. Thus, it would have been obvious to one skilled in the art at the time the invention was made to use to make fusion proteins of ligand linked to pVIII coat protein of a bacteriophage, such that multiple copies upto 3000 copies of the ligand are displayed on the surface of the phage.

15. Applicant's arguments filed on 8/11/03 regarding the rejection of claims over Schatz et al, Barbas III and specification disclosure have been fully considered but they are not persuasive.

Applicants arguments regarding the Babas III (US Patent 6,242,568 B1) are not persuasive. Applicants argue that the reference does not teach bacteriophage expression more than 10 copies of the polypeptide ligand. Applicants arguments have been fully considered and are not persuasive, since the reference in column 11 clearly discloses that gen VIII coat protein is present the mature filamentous phage typically about 2500 to 3000 copies of the coat protein. Thus, the reference clearly teaching the use of pVIII coat protein in the fusion protein such that large number of copies displayed. And further in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 U. S. P. Q. 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 U. S. P. Q. 375 (Fed. Cir. 1986). Schatz et al teach the use of bacteriophage vectors in detecting the polypeptide in the sample and the Babas III teach VIII coat protein' expression in multiple copies in mature phage and the specification discloses the use of pVIII coat protein in the fusion. Thus the teachings of reference in combination would read on the instant claimed invention.

16. The following is a statement of reasons for the indication of allowable subject matter: a method of detecting a NMDA receptor in a sample by contacting the sample with a virus

displaying a peptide of amino acid sequence of SEQ ID NO 2 or SEQ ID NO 3 is neither taught nor suggested by the prior art.

17. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner is on ***Increased Flex Schedule*** and can normally be reached on Monday to Friday between 7.00 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

P. Ponnaluri
Primary Examiner
Technology Center 1600
Art Unit 1639
03 November 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER